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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/523,455	03/10/2000	Jurgen Engel	PM 264671	5040

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PILLSBURY WINTHROP SHAW PITTMAN, LLP
P.O. BOX 10500
MCLEAN, VA 22102

EXAMINER	
JIANG, SHAOJIA A	

ART UNIT	PAPER NUMBER
1617	

DATE MAILED: 06/13/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/523,455	ENGEL ET AL.	
	Examiner	Art Unit	
	Shaojia A. Jiang	1617	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *01 April 2005*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1 and 4-24* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1 and 4-24* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office Action is in response to Applicant's amendment and response filed on April 1, 2005 wherein claims 2-3 are cancelled and claims 1 and 4-24 have been amended.

Currently, claims 1 and 4-24 are pending in this application.

Claims 1 and 4-24 as amended now are examined on the merits herein.

Applicant's amendment that limits claims 1, 4, 11, and 21, filed April 1, 2005 with respect to the rejection made under 35 U.S.C. 112 first paragraph for lack of scope of enablement of record stated in the Office Action dated October 4, 2004 has been fully considered and found persuasive to overcome the rejection since for the particular and specific LHRH-antagonists have been recited. Therefore, the said rejection is withdrawn.

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 1 and 4-24 are rejected under 35 U.S.C. 103(a) as being unpatentable over Engel et al. (EP 0788 799, of record) and Albano et al. (of record) and Felberbaum et al. (of record) and Garfield (5,470,847, of record) in view of Deghenghi (5,945,128, of

record) and Rabasseda et al. (of record) and Kent (4,016,259 of record) for reasons of record stated in the Office Action dated October 4, 2004.

Note that the amended claim 1 has changed the order of the stepwise method herein, i.e., step (a) as originally filed now become step (c). Thus, the order of the steps recited herein is **not** critical and essential in this method claimed herein.

Engel et al. discloses that an LHRH-antagonist, such as cetrorelix, is useful in the method of the treatment of infertility disorders, by inducing follicle growth by administering exogenous gonadotropins and in administering the LH-RH antagonist as low as only to suppress endogenous LH but the FSH secretion is maintained.. See abstract. Engel et al. also discloses the steps of suppressing premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques, e.g., ICSI or intrauterine insemination by sperm injection, with multiple follicle and oocyte development. See the abstract, col. 1 lines 10-20, 30-34, 39-59, col. 2 lines 1-13, 16-25, col.3 lines 1-12, and claims 1-14. Engel et al. also discloses exogeneous stimulation of the ovarian follicle growth and ovulation induction with HCG, LHRH, or LHRH-agonists and the stimulation is performed by administration of FSH or HMG with or without recombinant LH. See Abstract, col. 2 lines 38-43. Engel et al. further discloses the effective amount of LHRH-antagonist, cetrorelix, 0.1-5 mg, within the instant claim to be administered during luteal phase. See Examples claim 6-8. Finally, Engel et al. teaches progesterone is useful in supporting the beginning of pregnancy. See col.1 lines 23-24.

Albano et al. teaches that LHRH-antagonists, such as cetrorelix, are useful in the method of suppression of premature ovulation in controlled ovarian sitmulation and

assisted reproductive techniques, e.g., IVF and ICSI, with multiple follicle and oocyte development, as well as the effective amount of the LHRH-antagonist cetrorelix within the instant claim to be administered during luteal phase. See Abstract, Introduction and Results. Albano et al. further teaches that progesterone concentration is significantly lowered due to the administration of cetrorelix. See page 2115, 5th paragraph of right column.

Felberbaum et al. teaches that LHRH-antagonists, such as cetrorelix and ganirelix, are useful in the method of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques, e.g., IVF and ICSI, with multiple follicle and oocyte development, as well as the effective amount of the LHRH-antagonist cetrorelix within the instant claim to be administered during luteal phase. See Abstract, page 399-402 Felberbaum et al. further teaches a fall of sex steroids due to the administration of LHRH-antagonists. See page 398, the last three lines.

Garfield teaches that the administration of progestogen in the follicular phase is useful along with other progestins, an estrogen, e.g. ethinylestradiol, and an LHRH-antagonist in a method of controlling ovarian stimulation and preventing conception. See abstract, col.1 lines 18-67 and col.5 lines 35-38. Garfield also teaches that the ovarian stimulation is achieved with antioestrogens, such as clomiphene, combined with gonadotropins. See col. 2 lines 9-17, col.5 lines 64-67 and col.6 lines 30-40.

The prior art does not expressly disclose that the particular LHRH-antagonist are teverelix, antide, and abarelix and their effective amounts to be administered. The prior art does also not expressly disclose that the ovarian stimulation therapy may be on

Fridays to Mondays, and ooctye pick up and ART may be undertaken on Mondays to Thursdays. The prior art does not expressly further disclose the particular employment of oral contraceptive preparations containing progestogen and mestranol in the management of infertility.

Deghenghi discloses cetrorelix, teverelix, ganirelix and antide are known to be LHRH-antagonists. see col.2 lines 19-23.

Rabasseda et al. teach that LHRH-antagonists such as cetrorelix, ganirelix, and abarelix are known to be useful in the treatment of female infertility (see Introduction and Table 1 of page 397).

Kent discloses that the combination of progestogens and estrogen, i.e., mestranol and ethinylestradiol is useful in animal contraception (see col.1 lines 20-25).

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to employ the particular LHRH-antagonist such as teverelix, antide, and abarelix and to optimize their effective amounts to be administered, and to schedule or program the ovarian stimulation therapy on Fridays to Mondays and ooctye pick up and ART on Mondays to Thursdays, to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen.

One having ordinary skill in the art would have been motivated to employ the particular LHRH-antagonist such as teverelix, antide, and abarelix since teverelix, antide, and abarelix are known to be LHRH-antagonists, useful in the methods of controlled ovarian situmlation and assisted reproductive techniques and of the treatment

of infertility according to Engel et al., Albano et al., Felberbaum et al., Deghenghi and Rabasseda et al.

Additionally, one of ordinary skill in the art would have been motivated to optimize the effective amounts of active ingredients in the composition because the optimization of amounts of active agents to be administered is considered well within the skill of artisan. One having ordinary skill in the art would have been motivated to schedule or program the ovarian stimulation therapy on Fridays to Mondays and ooctye pick up and ART on Mondays to Thursdays since scheduling or programming the known ovarian stimulation therapy for Fridays to Mondays according to the calendar is considered well within the skill of artisan as the optimization of a result effective parameter, e.g., dosage regimen.

One having ordinary skill in the art would have been further motivated to employ the particular estrogen, mestranol, in oral contraceptive preparations along with progestogen in the management of infertility since the known contraceptive preparations of Kent contain mestranol and progestogen, and estrogen and progestin containing contraceptive agents are known broadly to be useful in the therapeutic management of infertility.

Since all method and composition components herein are known to be useful to treat or manage the infertility, it is considered prima facie obvious to combine them into a single method useful for the very same purpose. See *In re Kerkhoven*, 205 USPQ 1069 (CCPA 1980).

Response to Argument

Applicant's arguments filed on April 1, 2005 with respect to this rejection of claims 1 and 3-24 made under 35 U.S.C. 103(a) of record in the Office Action have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Again, Applicant's arguments that the cited references, either alone or in combination does not render the presently claimed invention unpatentable have been considered but are not found persuasive.

Applicant asserts the citation of seven different and unrelated documents. Contrary to Applicant's assertion, all cited references, especially all primary references, Engel et al., Albano et al., Felberbaum et al. and Garfield, clearly disclose methods of the treatment of infertility disorders and the methods of suppression of premature ovulation in controlled ovarian sitmulation and assisted reproductive techniques.

As discussed in the previously Office Action, the instant LHRH-antagonists such as teverelix, antide, and abarelix are known to be LHRH-antagonists and known to be useful in the methods of controlled ovarian situmlation and assisted reproductive techniques and of the treatment of infertility according to Engel et al., Albano et al., Felberbaum et al., Deghenghi and Rabasseda et al. Thus, each step in the instant claimed method is known in the prior art for treating or managing infertility.

As pointed out above, the amended claim 1 has changed the order of the stepwise method herein, i.e., step (a) as originally filed now become step (c). Thus, the order of the steps recited herein is indeed not critical and essential in this claimed

method. Therefore, one of ordinary skill in the art would employ each known step in treating or managing infertility by administering these known active agents.

It must be recognized that any judgment on obviousness takes into account only knowledge which was within the level of ordinary skill at the time the claimed invention was made. See MPEP 2145.

Further, the particular estrogen herein, mestranol, in oral contraceptive preparations in combination with progestogen are well known contraceptive agents and also known broadly to be useful in the therapeutic management of infertility according to the prior art. Therefore, one of ordinary skill in the art would have reasonably expected that combining these particular agents known useful for the same purpose in a composition to be administered would produce additive therapeutic effects to improve the treatment of in the therapeutic management of infertility, absent evidence to the contrary.

Since all active composition components herein are known to useful in the therapeutic management of infertility, it is considered prima facie obvious to combine them into a single composition to form a third composition useful for the very same purpose. At least additive therapeutic effects would have been reasonably expected based on the well settled principle set forth *In re Kerkhoven* regarding combination inventions. One cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. In re Keller, 642 F.2d 413, 208 SPQ 871 (CCPA 1981); In re Merck & Co., Inc., 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). See MPEP 2145.

Therefore, motivation to combine the teachings of the prior art cited herein to make the present invention is seen. The claimed invention is clearly obvious in view of the prior art.

Applicant's results of the instant method (program) in the specification at page 4-5 herein have been fully considered with respect to the nonobviousness and/or unexpected results of the claimed invention over the prior art but are not deemed persuasive for the reasons below. The results provide no clear and convincing evidence of nonobviousness or unexpected results over the cited prior art since there is no side-by-side comparison with the closest prior art. Therefore, the evidence presented in specification herein is not seen to support the nonobviousness of the instant claimed invention over the prior art.

For the above stated reasons, said claims are properly rejected under 35 U.S.C. 103(a). Therefore, said rejection is adhered to.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1 and 3-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,319,192.

Although the conflicting claims are not identical, they are not patentably distinct from each other because the patent is drawn to a method of therapeutic management of infertility by intrauterine insemination consisting of substantially similar method steps and administering the same pharmaceutical agents, i.e. an LHRRH-antagonist such as cetrorelix, HCG, native LHRH, LHRH-agonists or recombinant LH.

The claims of the instant application is drawn to the method of therapeutic management of infertility by programming of controlled ovarian stimulation and assisted reproductive procedures the improvement.

One having ordinary skill in the art would clearly recognize that the method in the patent and the method in the instant application consisting of substantially similar method steps and administering the same pharmaceutical agents are seen to substantially overlap.

Thus, the instant claims 1 and 3-24 are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-6 of U.S. Patent No. 6,319,192.

Response to Argument

Applicant's argument filed on April 1, 2005 with respect to this obviousness-type double patenting rejection have been fully considered but are not deemed persuasive as to the nonobviousness of the claimed invention over the prior art as further discussed below.

Applicant asserts that "[n]owhere in the disclosure of the '192 patent or over the claimed invention is there a teaching or suggestion regarding the importance of programming the COS/ART procedures by resetting the menstrual cycle using progestrogen or other oral conceptive preparations.

Contrary to Applicant's assertion, claim 1 is not limited to any the COS/ART procedures, and only a single claim 4 recites the COS/ART procedures. However, the COS/ART procedures are well known in the art. Hence, the major steps claimed herein have been disclosed in the patent. Therefore, said claims are properly rejected for obviousness-type double patenting and said rejection is adhered to.

In view of the rejections to the pending claims set forth above, no claims are allowed.

Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Examiner Jiang, whose telephone number is (571)272-0627. The examiner can normally be reached on Monday-Friday from 9:00 to 5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Sreenivasan Padmanabhan, Ph.D., can be reached on (571)272-0629. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

S. Anna Jiang, Ph.D.
Primary Examiner
Art Unit 1617
June 3, 2005